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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/643,579	08/22/2000	Richard Martin Broglie	BB1334 USNA CNT1	3114

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/643,579	BROGLIE ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25,29,37,39-44 and 49-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,25,29,37,39-44 and 49-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The rejection of Claims 1-9, 24-25, 29, and 36 under 35 U.S.C. 112, second paragraph is withdrawn in view of Applicants amendments.

Claims 1-22, 24, 26-28, 30-36, 38, 45-48 and 59 are cancelled. Claims 23, 25, 29, 37, 39-44 and 49-58 are pending and examined.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/26/2004 has been entered.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The title should reflect that the invention is directed to a method of increasing oleic acid content in seeds of transgenic comprising a mutant delta-12 enzyme with reduced linoleic acid in seed oil.

Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23, 25, 29, 37, 39-44 and 49-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a method for increasing oleic acid content in plant seeds by transformation with a delta-12 fatty acid desaturase coding sequence having a Asp/Glu to Lys mutation in a conserved (Ala/Gly)-His-(Asp/Glu)-Cys-Gly-His sequence and a recombinant construct effective for increasing oleic acid content when expressed in seeds comprising a coding sequence of a delta 12- fatty acid desaturase having a Asp/Glu to Lys substitution in a conserved His-(Asp/Glu)-Cys-(Gly/Ala)-His sequence that renders the desaturase non-functional.

Applicant describes a conserved His-Asp/Glu-Cys-Gly/Ala-His amino acid sequence (SEQ ID NO: 17) and the mutant delta-12 fatty acid desaturase polynucleotides of SEQ ID NO: 3 and 7 encoding the mutant delta-12 fatty acid desaturase amino acids of SEQ ID NO: 4 and 8.

Applicant does not describe any other mutant delta-12 fatty acid desaturase polynucleotides other than SEQ ID NO: 3 and 4 encoding amino acids of SEQ ID NO: 7 and 8.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a

genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a mutant delta-12 fatty acid desaturase protein comprising a conserved His-Asp/Glu-Cys-Gly/Ala-His amino acid sequence, wherein a Lys is substituted for a Asp/Glu falling within the scope of the claimed genus of polynucleotides to be used in the claimed method of increasing oleic acid content in a plant seed.

Based upon the disclosure of SEQ ID NO: 3 and 7, there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of polynucleotide sequences encoding a mutant delta-12 fatty acid desaturase protein comprising a conserved His-Asp/Glu-Cys-Gly/Ala-His amino acid sequence, wherein a Lys is substituted for a Asp/Glu, that increase the oleic acid content in transformed plant seeds, including additional mutants and allelic variants, absent further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered sequences that increase oleic acid content in transformed seeds, the disclosure of SEQ ID NO: 3 and 7 does not provide adequate description of the claimed genus. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession of the genus of polynucleotides encoding mutant delta-12 fatty acid desaturase proteins comprising a conserved His-Asp/Glu-Cys-Gly/Ala-His amino acid sequence, wherein a Lys is substituted for a Asp/Glu

other than SEQ ID NO: 3 and 7, that increase the oleic acid content of transformed seeds as broadly claimed.

Given the failure of the genus of polynucleotides encoding mutant delta-12 fatty acid desaturase proteins comprising a conserved His-Asp/Glu-Cys-Gly/Ala-His amino acid sequence, wherein a Lys is substituted for a Asp/Glu other than SEQ ID NO: 3 and 7, that increase the oleic acid content of transformed seeds to be adequately described, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-1111.

Claims 23, 25, 29, 37, 39-44 and 49-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing of oleic acid (18:1) in seeds of *Brassica napus* (var. Westar) transformed with the mutant delta-12 fatty acid desaturase genes of SEQ ID NO: 3 (pZPhMCFd2) and SEQ ID NO: 7 (pIMC140) (Example 4 pages 34-39) wherein the levels of oleic (18:1), linoleic 18:2) and linolenic (18:3) acid range from 72.5-78.6% for oleic acid, 6.4-10.6% for linoleic acid and 4.51-6.5% for linolenic acid respectively, does not reasonably provide enablement for a method of increasing levels of seed oleic as high as 90% recited in Claims 23 39 and 40, or 88% in Claims 41-42 for oleic acid; or as low as 1% linoleic acid recited in Claims 25 and 44, and as low as 1% linolenic acid recited in Claim 43. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by

one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims a method for increasing oleic acid content in plant seeds by transformation with a delta-12 fatty acid desaturase coding sequence having a Asp/Glu to Lys mutation in a conserved (Ala/Gly)-His-(Asp/Glu)-Cys-Gly-His sequence and a recombinant construct effective for increasing oleic acid content when expressed in seeds comprising a coding sequence of a delta 12- fatty acid desaturase having a Asp/Glu to Lys substitution in a conserved His-(Asp/Glu)-Cys-(Gly/Ala)-His sequence that renders the desaturase non-functional.

Applicant teaches a method of increasing of oleic acid (18:1) and lowering linoleic (18:2) and linolenic acid (18:3) in seeds of *Brassica napus* (var. Westar) transformed with the mutant delta-12 fatty acid desaturase genes of SEQ ID NO: 3 (pZPhMCFd2) and SEQ ID NO: 7 (pIMC140) (Example 4 pages 34-39) wherein the levels of oleic, linoleic and linolenic acid range from 72.5-78.6% for oleic acid, 6.4-10.6% for linoleic acid and 4.51-6.5% for linolenic acid respectively.

Applicant does not teach a method of increasing levels of seed oleic, and lowering linoleic and linolenic acid resulting in ranges of above 78.6% for oleic acid (18:1), and lower than 6.4% for linoleic acid (18:2), and lower than 4.51% for linolenic acid (18:3).

The state of the art for increasing oleic acid content and decreasing linoleic and linolenic acid content in the seeds of plants by blocking the conversion of oleic acid to linoleic and

linolenic acid by transformation with a mutant form of the endogenous delta 12 desaturase is unpredictable because this type of mutational inhibition or dominant negative inhibition of gene expression is leaky and requires multiple gene expression inhibition strategies to achieve levels of oleic acid in plant seeds such that seed oleic acid levels increase to 90% and linoleic and linolenic acid levels decrease to 1%. This is clearly made evident in a *Brassica napus* high oleic mutant homozygous for a mutant of delta 12 desaturase (IMC 129) resulting in a high seed oleic acid trait that required an additional antisense construct (158-8-1) to further inhibit delta 12 desaturase activity such that levels of seed oleic acid would increase to 90%. The data shows that seed oleic acid content in the cross of IMC 129 x 158-8-1 are higher than either parent (Lightner J.E. *et al.* U.S. Patent 6,372,965 B1, issued 2002; see column 65, Table 18; and column 66, Table 19 and lines 22-27). Further, Applicant's claim for a range of linolenic acid (i.e. 18:3) level in transformed seeds of 1-10% falls well above and below the range of the Westar wild type control seed (see column 62, Table 15 under westar control, row 18:3). It is not clear how the method could be enabled for both increasing and decreasing linolenic acid levels in seeds relative to wild type levels.

The state of the art for a method of increasing oleic acid content in seeds using a mutant or dominant negative protein comprising mutated conserved regions to eliminate gene expression is unpredictable because the resulting modified proteins can be either leaky resulting in an incomplete inhibition of gene expression, or produce mutant proteins that have the opposite effect. Previously identified mutations in ras p21 (Ala to Thr) showed a contrasting effect when transposed into a related alpha G protein (Gly225 to Thr). The corresponding Gly to Thr change made to the alpha subunit only eliminated 70% of the activity compared to the wild type protein

(Osawa S. *et al.* Journal of Biological Chemistry, March 15, 1991; Vol. 266, No. 8, pp. 4673-4676; see page 4674, column 1 line 12 to column 2 end of paragraph). Thus, unknown regulatory or structural properties of a homologous protein can have unexpected results when attempting to engineering analogous activities into related proteins by transposing peptide modifications.

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified transformed plants comprising any one of a myriad of delta 12 desaturase proteins comprising a mutant delta-12 sequence having a Lys substituted for a Asp/Glu in a (Ala/Gly)-His-(Asp/Glu)-Cys-Gly-His conserved sequence to identify those polynucleotides that when transformed and expressed in plants produce plants having seeds with increased oleic acid levels as high as 90% and linoleic and linolenic acid levels as low as 1%.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the broad scope of the claims.

All claims are rejected.

Claims 23, 25, 29, 37, 39-44 and 49-58 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a recombinant nucleic acid construct effective for increasing oleic acid content in a plant when expressed in seeds comprising a mutation wherein a Lys residue is substituted for a Glu or Asp in a conserved His-Asp/Glu-Cys-Gly/Ala-His sequence of a delta-12 fatty acid desaturase, and a method of increasing oleic acid content in a seed of a plant transformed therewith.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis

Russell Kallis Ph.D.
September 26, 2004